

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 2

Attorney's Docket No.: 09010-027003

AMENDMENT

Please amend the application as follows:

In the claims:

Please cancel claim 52.

Please replace claim 31 with amended claim 31 as follows:

B1
Sub C1

-- 31. (Twice Amended) A method of generating a variant that encodes a polypeptide having polymerase activity comprising:
obtaining a nucleic acid comprising a sequence having at least 70% identity to the sequence set forth in SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or its complement; and
modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence, to generate a variant that encodes a polypeptide having polymerase activity. --

Please add claims 53-88.

Sub C1
B2

-- 53. (New) A method of generating a variant that encodes a polypeptide having polymerase activity comprising:
obtaining a nucleic acid comprising a sequence as set forth in SEQ ID NO:1, or its complement; and
modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence, to generate a variant that encodes a polypeptide having polymerase activity.

54. (New) The method of claim 53, wherein the modifications are introduced by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo*

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 3

Attorney's Docket No.: 09010-027003

mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, ligation reassembly, gene site saturated mutagenesis (GSSM) and any combination thereof.

55. (New) The method of claim 53, wherein the modifications are introduced by error-prone PCR.

56. (New) The method of claim 53, wherein the modifications are introduced by shuffling.

57. (New) The method of claim 53, wherein the modifications are introduced by oligonucleotide-directed mutagenesis.

58. (New) The method of claim 53, wherein the modifications are introduced by assembly PCR.

59. (New) The method of claim 53, wherein the modifications are introduced by sexual PCR mutagenesis.

60. (New) The method of claim 53, wherein the modifications are introduced by *in vivo* mutagenesis.

61. (New) The method of claim 53, wherein the modifications are introduced by cassette mutagenesis.

62. (New) The method of claim 53, wherein the modifications are introduced by recursive ensemble mutagenesis.

63. (New) The method of claim 53, wherein the modifications are introduced by exponential ensemble mutagenesis.

B2
Cont.

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 4

Attorney's Docket No.: 09010-027003

64. (New) The method of claim 53, wherein the modifications are introduced by site-specific mutagenesis.

65. (New) A method of generating a variant that encodes a polypeptide having polymerase activity comprising:

obtaining a nucleic acid comprising a fragment of at least 30 consecutive nucleotides of a sequence having at least 70% identity to the sequence set forth in SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or its complement; and
modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence, to generate a variant that encodes a polypeptide having polymerase activity.

66. (New) The method of claim 65, wherein the modifications are introduced by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, ligation reassembly, gene site saturated mutagenesis (GSSM) and any combination thereof.

67. (New) The method of claim 65, wherein the modifications are introduced by error-prone PCR.

68. (New) The method of claim 65, wherein the modifications are introduced by shuffling.

69. (New) The method of claim 65, wherein the modifications are introduced by oligonucleotide-directed mutagenesis.

B2
Cont

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 5

Attorney's Docket No.: 09010-027003

70. (New) The method of claim 65, wherein the modifications are introduced by assembly PCR.

71. (New) The method of claim 65, wherein the modifications are introduced by sexual PCR mutagenesis.

72. (New) The method of claim 65, wherein the modifications are introduced by *in vivo* mutagenesis.

73. (New) The method of claim 65, wherein the modifications are introduced by cassette mutagenesis.

74. (New) The method of claim 65, wherein the modifications are introduced by recursive ensemble mutagenesis.

75. (New) The method of claim 65, wherein the modifications are introduced by exponential ensemble mutagenesis.

76. (New) The method of claim 65, wherein the modifications are introduced by site-specific mutagenesis.

77. (New) A method of generating a variant that encodes a polypeptide having polymerase activity comprising:

obtaining a nucleic acid comprising a fragment of at least 30 consecutive nucleotides of a sequence as set forth in SEQ ID NO:1 and encoding a polypeptide having polymerase activity or its complement; and

modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence, to generate a variant that encodes a polypeptide having polymerase activity.

32
Cont.

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 6

Attorney's Docket No.: 09010-027003

78. (New) The method of claim 77, wherein the modifications are introduced by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, ligation reassembly, gene site saturated mutagenesis (GSSM) and any combination thereof.

79. (New) The method of claim 77, wherein the modifications are introduced by error-prone PCR.

80. (New) The method of claim 77, wherein the modifications are introduced by shuffling.

81. (New) The method of claim 77, wherein the modifications are introduced by oligonucleotide-directed mutagenesis.

82. (New) The method of claim 77, wherein the modifications are introduced by assembly PCR.

83. (New) The method of claim 77, wherein the modifications are introduced by sexual PCR mutagenesis.

84. (New) The method of claim 77, wherein the modifications are introduced by *in vivo* mutagenesis.

85. (New) The method of claim 77, wherein the modifications are introduced by cassette mutagenesis.

B2
Cont

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
Page : 7

Attorney's Docket No.: 09010-027003

86. (New) The method of claim 77, wherein the modifications are introduced by recursive ensemble mutagenesis.

87. (New) The method of claim 77, wherein the modifications are introduced by exponential ensemble mutagenesis.

88. (New) The method of claim 77, wherein the modifications are introduced by site-specific mutagenesis --

B²
cont

add C17